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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/666,851	09/19/2003	Peter Bodine	00630/100M091-US2	6790

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EXAMINER	
XIE, XIAOZHEN	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 05/19/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/666,851	BODINE, PETER	
	Examiner	Art Unit	
	Xiaozhen Xie	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-43* is/are pending in the application.

4a) Of the above claim(s) *7-19 and 26-43* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 20-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 February 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 10/169,545.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *20040212*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments, And/Or Claims

The Information Disclosure Statement (IDS) filed 12 February 2004 has been entered. Applicant's amendments of the claims filed on April 11 2006, and the specification filed on April 20 2006 are acknowledged.

Election/Restriction

Applicant's election with traverse of Group I, claims 1-6 and 20-25, and species A-b), an antibody against an sFRP or portions thereof, in the reply filed on 11 April 2006 is acknowledged. The traversal is on the ground(s) that Group I drawn to a pharmaceutical composition for regulating bone-forming activity in a mammal and Group II drawn to a method for treating or preventing a bone disorder are related as product and process of use, and therefore, examination of Groups I and II together would not impose an undue burden on the Examiner. Applicant's arguments have been fully considered but have not been found to be persuasive. As described in the Office Action of 13 March 2006, MPEP states that the inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the composition comprising the antibody can be used in a materially different method, such as isolating a ligand.

The requirement is still deemed proper and is therefore made FINAL. Claims 1-43 are pending. Claims 7-19 and 26-43 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Claims 1-6 and 20-25 are under examination to the extent they read on the elected species.

Specification

The disclosure is objected to because of the following informalities: the amendment of the specification filed on April 20 2006 recites "U.S. Patent Application No: 09/394,832, filed September 13, 1999, no abandoned". It appears to be "now abandoned". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6 and 20-24 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are directed to a pharmaceutical composition for regulating bone-forming activity in a mammal comprising an antibody against a secreted frizzled related protein (sFRP) or regulating portion thereof. What applicant has

described in the specification is an antibody that specifically binds to a polypeptide, sFRP-1 of SEQ ID NO: 2 encoded by a polynucleotide of SEQ ID NO: 1. Applicant has not described other antibodies against fragments of sFRP, or against sFRPs of any species that have the binding specificity to sFRP1. There is no teaching regarding the relationship of structure to function, such as what amino acid sequences or regions are necessary and sufficient for specific antigen binding. Further, the specification also does not disclose a representative number of species of sFRPs commensurate with the scope of the genus of sFRP recited in claims 1 and 20 (fish sFRP, chicken sFRP, etc.). Thus, the claims encompass a genus of molecules, which vary substantially in composition, and could have very different structural and functional characteristics from the composition that Applicant has disclosed.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making of the claimed product, or any combination thereof. In this case, there is not even identification of any particular portion of the structure that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing

date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of peptides, and therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that is part of the invention and reference to a method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only a pharmaceutical composition comprising an antibody that specifically binds to a polypeptide, sFRP-1 of SEQ ID NO: 2, encoded by a polynucleotide of SEQ ID NO: 1, but not the full scope of the claimed sFRPs and fragments thereof, are adequately described in the disclosure.

Claims 1-6 and 20-24 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a pharmaceutical composition

comprising an antibody that specifically binds to a polypeptide, sFRP-1 of SEQ ID NO: 2, encoded by a polynucleotide of SEQ ID NO: 1, does not reasonably provide enablement for pharmaceutical compositions comprising antibodies against fragments of sFRP of any species. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The claims are directed to a pharmaceutical composition for regulating bone-forming activity in a mammal comprising an antibody against a secreted frizzled related protein (sFRP) or regulating portion thereof. The claims are broad in that they encompass or require the use of antibodies against fragments of sFRP of any species. The specification discloses an antibody that specifically binds to a polypeptide, sFRP-1 of SEQ ID NO: 2, encoded by a polynucleotide of SEQ ID NO: 1. The specification, however, does not provide any guidance for making or using other antibodies against fragments of sFRP, or against sFRPs of any species that have the binding specificity to sFRP-1. There is no teaching in the specification as to the relationship of structure to function, such as what amino acid sequences or regions are necessary and sufficient for specific antigen binding, or that would destroy the characteristics of the molecule. For example, Specht et al. (DE19813835-A1) teach a human breast tumor-associated protein 38, which comprises the amino acids 217-231 of SEQ ID NO: 2 of the instant application, and would bind to an antibody encompassed by the claims (see sequence alignment). Further, the specification also does not disclose a representative number of species of sFRPs commensurate with the

scope of the genus of sFRP recited in claims 1 and 20 (fish sFRP, chicken sFRP, etc.). Since the specification does not define where and what these fragments will be, one of skill in the art would evaluate all non-exemplified sFRP fragments for binding specificity to sFRP-1. Thus, undue experimentation would be required for the artisan to make and use the invention as broadly claimed.

Due to the large quantity of experimentation necessary to generate the nearly infinite number of sFRP fragments recited in the claims and screen same for binding specificity to sFRP-1, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide specificity, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes that particular amino acid sequences may be critical determinants of antigenicity, and the breadth of the claims which fails to recite any structural limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 3-6 and 20-24 are rejected under 35 U.S.C. 102(e) as being anticipated by Umansky et al. (U. S. Patent No: 6,433,155B1, which was filed on 24 September 1997). The '155 patent teaches a pharmaceutical composition comprising an antibody against a polypeptide of the SARP (Secreted Apoptosis-Related Protein) family including msarp1 from murine, hsarp2, hsarp1 and hsarp3 from human (column 3, lines 22-28, and column 4, lines 51-58). SARP-2 is also known as sFRP-1. The'155 patent teaches that SARP polypeptides can be isolated from biological sources (column 15, lines 13-15), and that hsarp2 is expressed in a variety of tissues (column 4, lines 57-58). The SARP polypeptide shares a 99.7% similarity to the sFRP protein of SEQ ID NO: 2 of the instant application, and has 100% identity in the amino acid sequence of residues 217-231 (see sequence alignment). While the'155 patent does not expressly teach that the pharmaceutical compositions are for regulating bone-forming activity in a mammal, this function would reasonably be considered to be inherent to the composition since it has exactly the same components recited in the claims. A compound and all of its properties are inseparable (*In re Papesch*, 315 F.2d 381, 137 USPQ 43 (CCPA 1963)).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Umansky et al. (U. S. Patent No: 6,433,155B1), in view of Hoang et al. (J. Biol. Chem., 1996, Vol. 271(42):26131-26137).

The '155 patent teaches as set forth above, a pharmaceutical composition comprising an antibody against a polypeptide of sFRP.

The '155 patent, however, does not teach that sFRP is from human osteoblast cells (claim 2), nor wherein the bone-forming activity is the regulation of bone growth (claim 3) or bone density (claim 4).

Hoang et al. teach tissue distribution of Frzb-1 (sFRP-3) in human embryos. Hoang et al. found that Frzb-1 is expressed in bone cells, and that Frzb-1 plays a role in skeletal morphogenesis (Figures 5-7, and pp. 26137, left column, last paragraph in Discussion section).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of the '155 patent, with those of Hoang et al. to isolate sFRP protein from human osteoblast cells, and to use the composition comprising an antibody thereto for regulating bone-forming activity in a mammal. One of ordinary skill in the art would have been motivated to combine the teachings, because the '155 patent teaches such composition comprising an antibody against sFRP which can be prepared from recombinant expression or from biological resources, Hoang et al. teach that sFRP is expressed in human bone cells, and plays a role in bone morphogenesis. Therefore, the combined teachings provide a reasonable

expectation of successfully regulating bone-forming activity using the composition.

Claim Objections

Claim 1 is objected to because of the following informalities: the claim recites non-elected species. Appropriate correction is required.

Claim 25 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

NO CLAIM IS ALLOWED.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Xiaozhen Xie, Ph.D whose telephone number is 571-272-5569. The examiner can normally be reached on M-F, 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary B. Nickol, Ph.D. can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Xiaozhen Xie, Ph. D.
May 11, 2006

GARY B. NICKOL, PH.D.
PRIMARY EXAMINER